Prime 2.1

Quick Start Guide

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Contents

Document Conventions

In addition to the use of italics for names of documents, the font conventions that are used in this document are summarized in the table below.

Font	Example	Use
Sans serif	Project Table	Names of GUI features, such as panels, menus, menu items, buttons, and labels
Monospace	`$SCHRODINGER/maestro`	File names, directory names, commands, environment variables, and screen output
Italic	*filename*	Text that the user must replace with a value
Sans serif uppercase	CTRL+H	Keyboard keys

Links to other locations in the current document or to other PDF documents are colored like this: Document Conventions.

In descriptions of command syntax, the following UNIX conventions are used: braces `{ }` enclose a choice of required items, square brackets `[ ]` enclose optional items, and the bar symbol | separates items in a list from which one item must be chosen. Lines of command syntax that wrap should be interpreted as a single command.

File name, path, and environment variable syntax is generally given with the UNIX conventions. To obtain the Windows conventions, replace the forward slash / with the backslash \ in path or directory names, and replace the $ at the beginning of an environment variable with a % at each end. For example, `$SCHRODINGER/maestro` becomes `%SCHRODINGER%\maestro`.

In this document, to *type* text means to type the required text in the specified location, and to *enter* text means to type the required text, then press the ENTER key.

References to literature sources are given in square brackets, like this: [10].

Introduction

This manual provides a tutorial introduction to using the Prime protein structure prediction suite. It includes tutorial exercises for the Prime–Structure Prediction Comparative Modeling Path. For a tutorial introduction to the Induced Fit Docking protocol, which uses Prime and Glide, see the document *Induced Fit Docking*.

Maestro is the graphical interface for Schrödinger products. The two Prime modules, Prime–Structure Prediction and Prime–Refinement, are run from Maestro panels which are opened from the Maestro Applications menu. Prime also uses the main Maestro window to display 3D structures and the Maestro Project Facility to handle information about the structures it produces. For an overview of Maestro, see the *Maestro Overview*. For more information on using Maestro, see the Maestro online help or the *Maestro User Manual*.

The Prime modules are briefly described in the tutorial chapters. For more information about Prime features, see the *Prime User Manual*.

It is assumed that you have already installed Maestro 9.0, Prime 2.1, and supporting third-party programs and databases (PDB, BLAST, HMMER/Pfam) from the Schrödinger CDs. In addition, it is assumed that you have downloaded and installed the optional (but highly recommended) third-party secondary structure prediction program PSIPRED. To find out how to obtain third-party programs, go to the Third Party Programs page of our website.

Before you can do the tutorial exercises, you must first set the `SCHRODINGER` environment variable to the installation directory for your Schrödinger software. To set this variable, enter the following command at a shell prompt:

csh/tcsh: `setenv SCHRODINGER` *installation-directory*

bash/ksh: `export SCHRODINGER=`*installation-directory*

Once you have set the `SCHRODINGER` environment variable, you can start Maestro with the following command:

```
$SCHRODINGER/maestro &
```

It is usually a good idea to change to the desired working directory before starting Maestro. This directory then becomes Maestro's working directory. For more information on starting Maestro, including starting Maestro on a Windows platform, see Section 2.1 of the *Maestro User Manual*.

Comparative Modeling Tutorial

Below is a step-by-step tutorial that takes you through the Comparative Modeling path of Prime–Structure Prediction and demonstrates the use of stand-alone Prime–Refinement. You will be building and refining a model of a query sequence for which a sequence homolog can be identified using BLAST. While the tutorial is self-contained, you may find it useful to refer to the *Prime User Manual* or the online help (click the Help button in any Prime panel) for more detailed information about the individual programs that make up the Comparative Modeling path. If you have not already done so, set the Schrödinger environment variable and start Maestro. See Chapter 1 for instructions.

2.1 Importing the Query Sequence

The query sequence that will be used is closely related to that of phosphoglycerate kinase from *Pyrococcus furiosus*, but has been modified slightly to provide a case that best demonstrates various features of Prime's Comparative Modeling path:

```
>Query
YNRTVFLRVDLNSPMSNGKVQSDARFRAVLPTIKYLIESGAKVVVGTHQGKEYSTTEEHARILSELLNMH
VEYVEDYAIFGISKARERAAMKPGEVIVLENLRFSAEEFVRKLSQVIDLVVNDAFAAAHRSQPSLVGFAR
IKPMIMGFL
```

In this section, you will copy the query sequence from the tutorial directory and import it into Prime as the first step of the Structure Prediction workflow.

1. Copy the sequence file for this tutorial into your working directory:

   `cp $SCHRODINGER/psp-v`*version*`/tutorial/PrimeTutorial1.fasta` *dir*

2. Start Maestro by entering the command:

   `$SCHRODINGER/maestro &`

3. On the main toolbar, click the Save as button:

   

   The Save As Project dialog box is displayed.

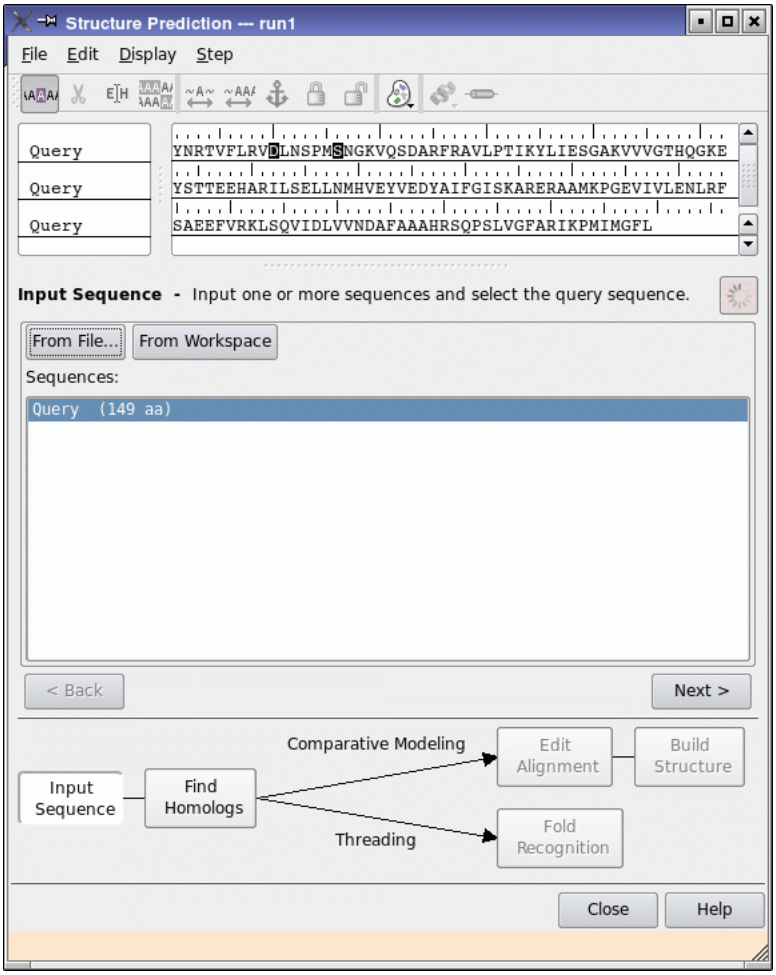

Figure 2.1. The Input Sequence step after import.

4. Type `PrimeTutorial1` in the Project text box, and click Save.

   You are now working in a named project (not a scratch project) called PrimeTutorial1.prj.

5. Choose Applications > Prime > Structure Prediction in the main window.

   The Structure Prediction panel opens at the first step, Input Sequence.

6. Click From File and select `PrimeTutorial1.fasta`, then click Open.

   The sequence is displayed in the Prime sequence viewer (Figure 2.1). At this stage, there is no structure to display in the Workspace.

Unlike the Prime sequence viewer, the Workspace sequence viewer in the lower part of the Maestro main panel displays sequences only for named entries in a project. Until the end of this tutorial, when the finished structure is added to the Project Table, the Workspace sequence viewer remains empty.

7. Click Next to proceed to the next step, Find Homologs.

2.2 Finding Sequence Homologs

In this step, you will search for homologous proteins with known structure using BLAST, then select one homolog as a template.

1. Click Search.

   The Find Homologs Run Search job is started.

This search usually takes less than 1 minute on a 1-GHz processor. When the job finishes, a list of potential templates is displayed in the Homologs table. The highest-scoring template is selected by default, as shown in Figure 2.2.

The PDB and BLAST databases provided are continually being updated. Therefore, the rank order and scores of the homologs found might differ slightly from that shown.

2. If the SSA is not visible in the sequence viewer, click the View SSA button on the toolbar.

   

   This button displays the secondary structure assigment in the sequence viewer. If it was not selected, when you select it the assignment for the homolog is displayed in the sequence viewer, with `_ssa` added to the homolog name.

3. Select the 1VPE_A template (by clicking its row).

   This template should be near the top of the Homologs table.

   The BLAST alignment between the template and query sequences is displayed in the Prime sequence viewer, along with the secondary structure assignment of the template. In addition, the selected template is displayed in the Workspace.

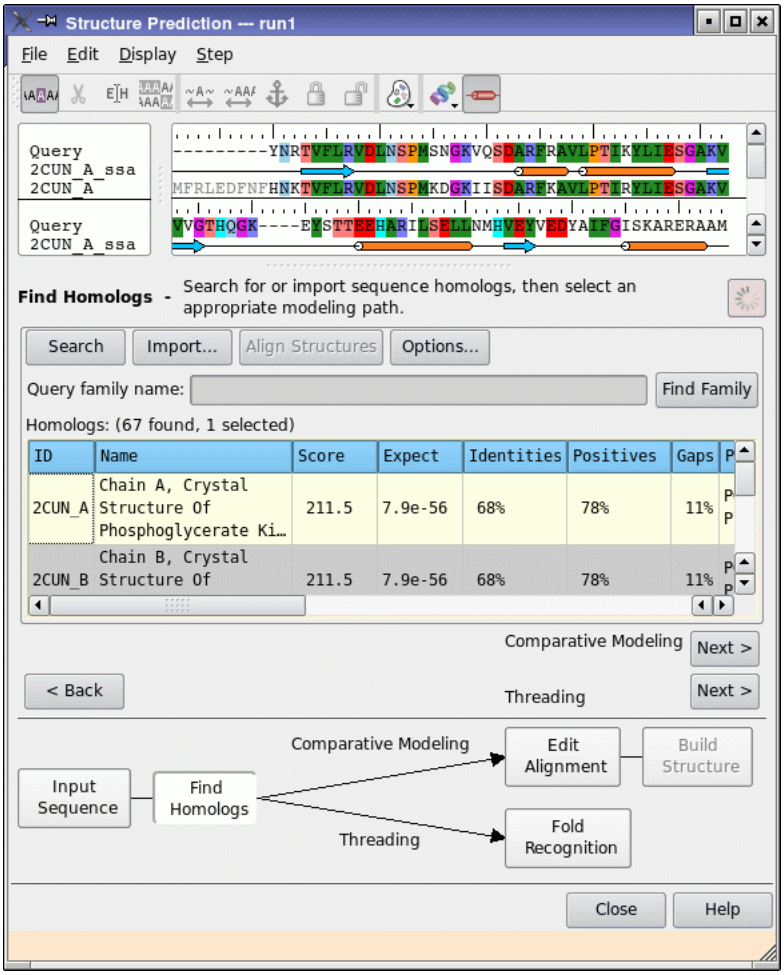

Figure 2.2. The Find Homologs step after searching for homologs.

4. Zoom in on the region of the template that is aligned to the query (the colored region of the ribbon representation.) and manipulate the view to resemble Figure 2.3.

5. Once you are satisfied with the view, save the view so you can easily return to it. To do this, click the Save View button on the Maestro toolbar:

Figure 2.3. The 1VPE_A template, showing the region aligned with the query.

(Optional) To obtain HMMER/Pfam family and sequence data:

1. Click Find Family.

   This job should take 2 to 3 minutes to complete. A Hidden Markov Model (HMM) is generated from a multiple sequence alignment and used to identify the query family and provide information about which residues are conserved in the consensus sequence.

   When the job finishes, the family appears in the Query family name text box, and the sequence is displayed in the sequence viewer, labeled `Query_pfam`.

   A minus sign appears beside the query name in the sequence viewer: this is a collapse/expand "button". Clicking on the minus sign hides the Pfam sequence, and the minus sign becomes a plus sign; clicking on the plus sign displays the Pfam sequence again.

2. Choose Legend from the Display menu or from the right-click menu in the sequence viewer.

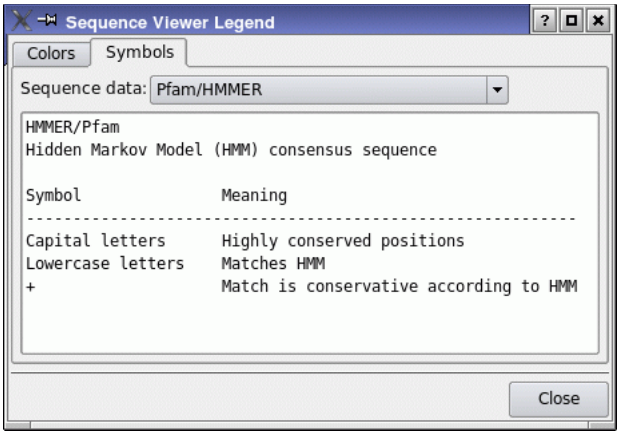

Figure 2.4. The Sequence Viewer Legend panel.

The Sequence Viewer Legend panel is displayed.

3. Click the Symbols tab and select Pfam/HMMER from the Sequence data menu.

   The key for the HMM consensus sequence is displayed in the center of the tab. The explanation of the symbols is as follows

Capital letters	Highly conserved positions
Lowercase	Matches HMM
+	Match is conservative according to HMM
Blank	Does not match HMM

4. Click Close.

To continue to the next step in the Comparative Modeling path:

1. Ensure that 1VPE_A is still selected.
2. Click the Next button to the right of the words Comparative Modeling.

   The next step is Edit Alignment. The template is again automatically fit to fill the Workspace.

3. To return the view to the one you saved in the previous step, click the Restore view button on the Maestro toolbar.

2.3 Editing the Alignment

Because the alignment provided by the Find Homologs step is based only on sequence information, there is room for improvement. For example, the default alignment has placed a gap at query residue His59, which corresponds to the middle of a helix in the template (Figure 2.5). Therefore, it is unlikely that the alignment returned by BLAST is correct in this region. This can be rectified either by hand-editing the alignment or by using the Prime Align program, which takes secondary structure into account.

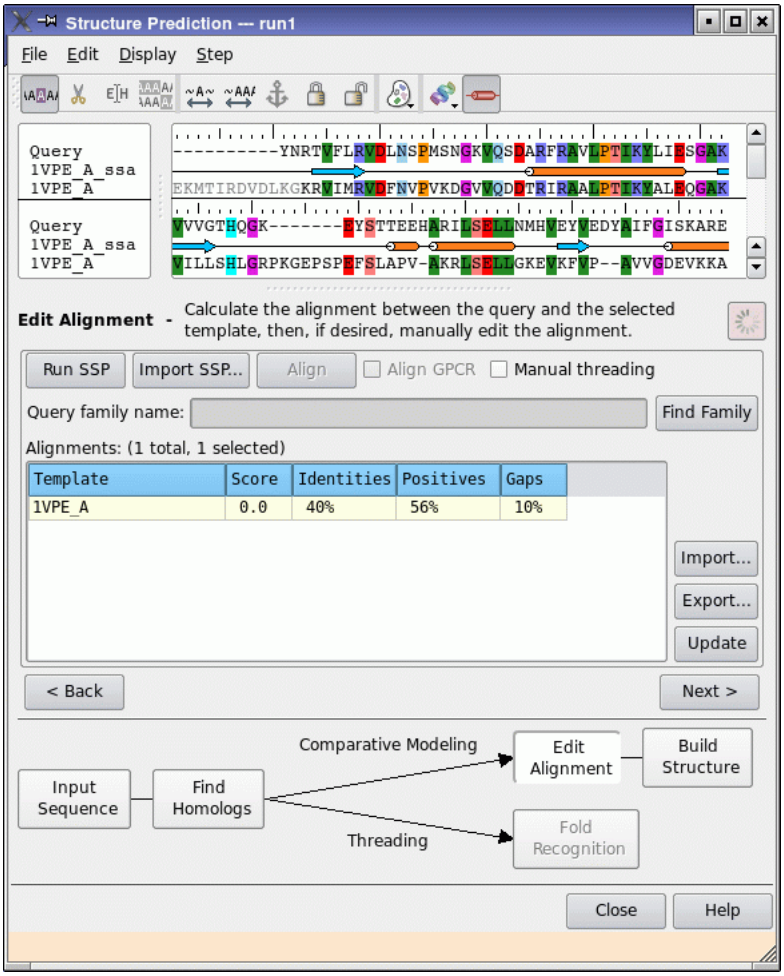

Figure 2.5. Initial view of the Edit Alignment step.

Before making changes to the BLAST alignment, save the current run:

1. From the File menu, choose Rename.
2. Enter `Blast_Alignment` in the dialog box, then click OK.

Name the new run you will be working in:

3. From the File menu, choose Save As.
4. Type `New_Alignment` in the text box and click OK.

   The `New_Alignment` run is the one that is now open. The `Blast_Alignment` run has been closed, but can be reopened at any time.

In order to deal with the fact that secondary structure prediction is only about 75% accurate,[1] Prime supports running two distinct secondary structure prediction programs. One of these, SSpro, is bundled with Prime. However, the other, PSIPRED, is not. If you have not already done so, you can find out how to obtain third-party programs from the Third Party Programs page of our website.

Now generate secondary structure predictions for the query to help guide the Align program:

5. Click Run SSP to run all available SSP programs.

   If the optional SSP program PSIPRED was installed (strongly recommended), this job should take about 5 minutes.

   Once the SSP job is completed (when the job status button turns pink and stops spinning), the secondary structure predictions of the query are displayed in the sequence viewer, as in Figure 2.6.

This and subsequent operations may produce different views of the structure in the Workspace. Click Restore view as needed.

6. Click Align.

   The Prime Align program starts running. This job may take 20 minutes to complete.

   Once the Align job finishes, the new alignment is displayed in the sequence viewer and the values in the Alignments table are updated. The template's Score, which was 0.0 prior to running the Align job, is now a non-zero number. In addition to some other minor changes in the alignment, the gap at His59 has been moved to an adjacent loop. This makes more physical sense and is likely to result in a more accurate homology model.

1. For example, visit the EVA site at http://cubic.bioc.columbia.edu/eva/sec/res_sec.html for more details

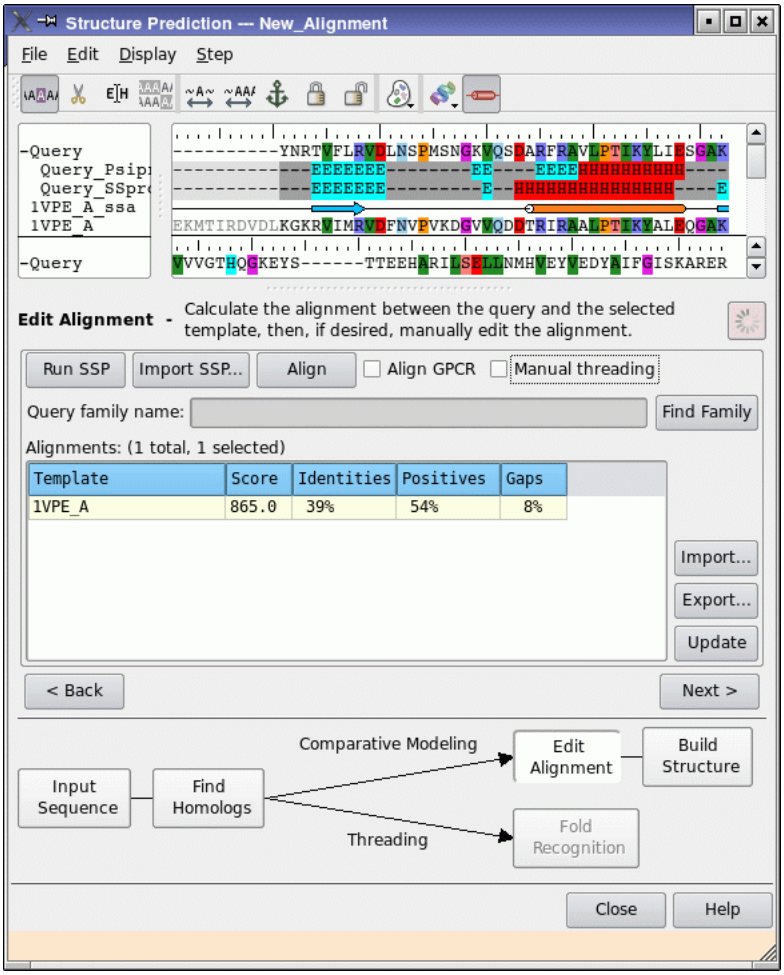

Figure 2.6. The Edit Alignment step after running SSP and Align.

7. (Optional) The true secondary structure of the template is shown graphically in the sequence viewer above the template sequence. To get an indication of the accuracy of the SSP programs in particular regions of the sequence, run the SSP programs on the template: right-click on the template in the sequence viewer and choose Run SSP from the menu.

While the Align program took secondary structure into account in producing the alignment between query and template, it did not explicitly consider tertiary structure. You will next perform some manual editing of the alignment that accounts for tertiary structure.

8. Select Manual Threading to enter the Manual Threading mode.

   Aligned residues in the template in the Workspace are now colored according to the query's Residue Property (Figure 2.7). That is, they are colored according to the residue type to which they will be converted once the model is built. Residues that are not being used in the current alignment are undisplayed, revealing where gaps exist in the alignment.

9. Examine the structure to confirm that hydrophobic residues (green) are directed toward the interior of the protein and charged residues (negative: red, positive: blue) are directed toward solvent (polar uncharged residues are colored cyan).

   The only exception is Helix 97-104 (template numbering), shown in Figure 2.7. To find this helix in the Workspace:

   a. Scroll the Prime sequence viewer to the second row.

   b. Locate the residue labeled (98) Asp97 by moving the pointer over the residues in the sequence viewer for the template.

   c. Drag to select the residues in the template from (98) Asp97 to (105) Glu104.

   The selected residues are highlighted in the Workspace with yellow markers.

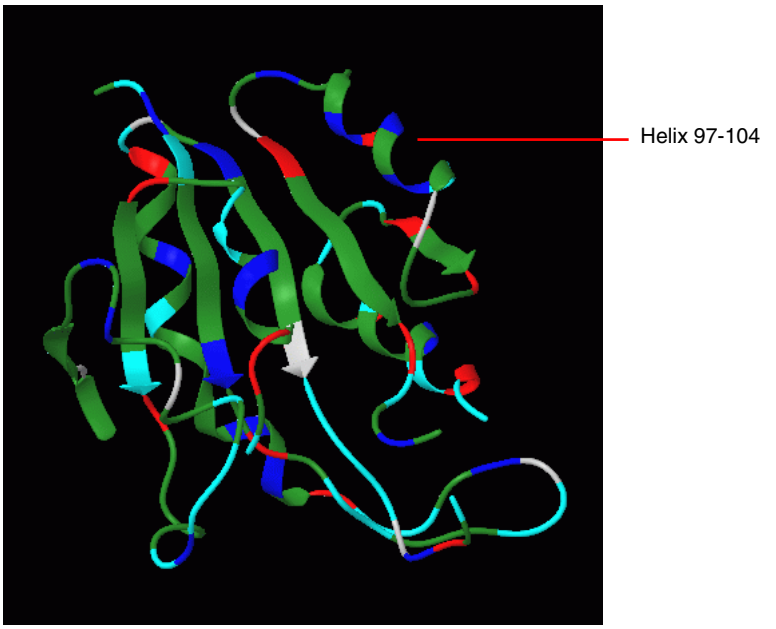

Figure 2.7. The template colored by the query's residue property.

10. Remove the markers by clicking in a blank area in the sequence viewer or the Workspace.

Several charged residues appear to be directed towards the interior of the protein, which is likely to result in buried charges in the model once built. This problem can be rectified by manually editing the alignment in this region. Fortunately, there is a two-residue gap near the helix that allows for some flexibility in the local alignment.

11. Change to Slide Freely mode by clicking Slide Freely on the Prime toolbar:

12. Drag residue Leu106 (of the template) to the left by two positions.

    The original gap is closed, and a new C-terminal gap is created.

13. Click Update to view the effect of the change in the Workspace.

    The problematic charged residues are now mapped to residues directed outward, which is more physically reasonable (see Figure 2.8).

Now that an optimal alignment between query and template has been generated, you can proceed to the next step.

14. Click Next to proceed to the Build Structure step.

Figure 2.8. Helix from Figure 2.7 after hand editing in Manual Threading mode.

2.4 Building a Model Structure

The Build Structure program builds insertions, closes gaps, and predicts side-chain conformations of non-conserved residues to produce a model with no unphysical clashes. However, it does this efficiently, without extensive conformational sampling. The structure produced in the Build Structure step is likely to represent only a local energy minimum and not the global minimum. Therefore, regions with gaps in the alignment are likely to require refinement in the refinement step.

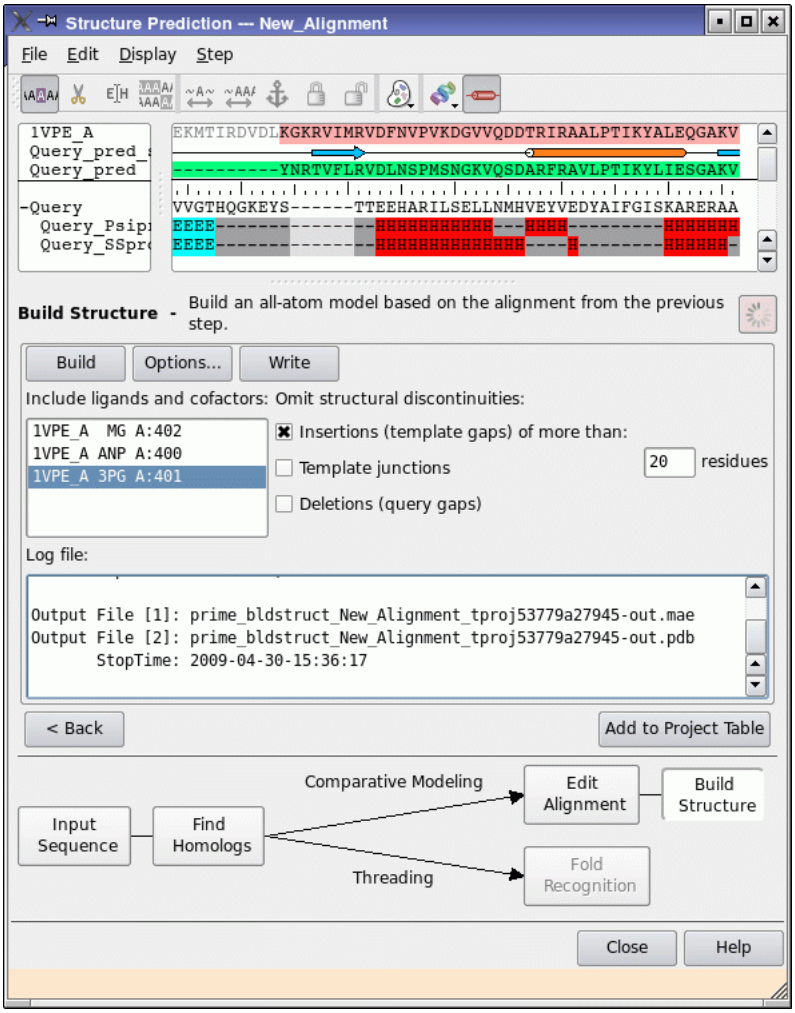

Figure 2.9. The Build Structure step after building.

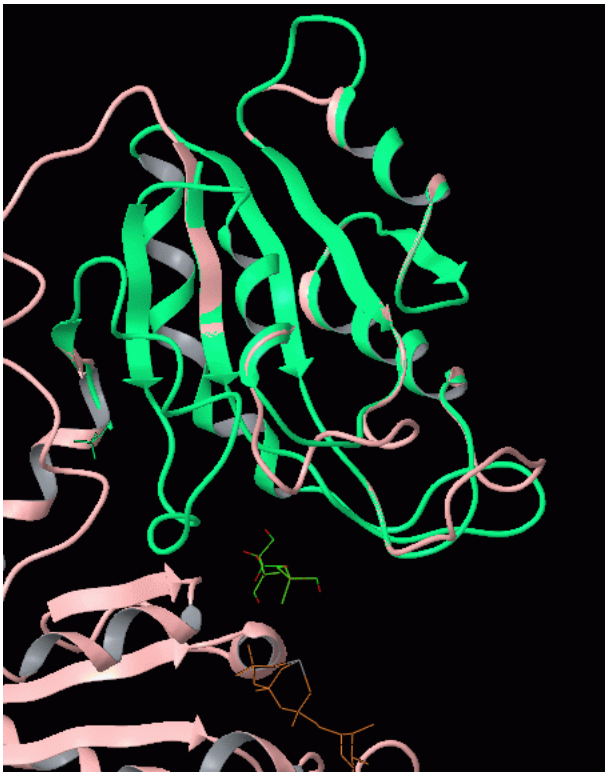

Figure 2.10. Workspace after building structures.

In this part of the exercise, you will construct a homology model that is based on the alignment produced in the previous step and that includes the template ligand 3PG.

1. Select the ligand 3PG from the Include ligand and cofactors list .

   The selected ligand is highlighted in the Workspace.

2. Click Build.

   This job takes about 15 minutes on a 1-GHz processor.

   Once the model-building calculation is complete, the model is displayed in the Workspace superimposed on the template (Figure 2.10).

3. When the job finishes, click Add to Project Table.

   The Project Table panel opens with the selected structure as an entry.

4. Close the Structure Prediction panel.

5. Click the In column in the Project Table panel to include the entry in the Workspace.

   The predicted structure is incorporated into the Project Table and is displayed in the Workspace.

Structures visible in the Workspace while working in the Structure Prediction interface are scratch entries (not yet part of the Project Table.) The Workspace sequence viewer does not display scratch entries. Now that this structure is a Project Table entry, its sequence and SSA are displayed in the Workspace sequence viewer. The Workspace sequence viewer is not displayed by default. To display it, choose View > Sequence Viewer from the main window.

2.5 Refining Target Regions of the Structure

2.5.1 Refining Loops

To improve the structure most efficiently, you should focus refinement efforts on areas of the structure that are likely to be problematic. In general terms, this means refining loops (particularly where insertions have been made or gaps closed) and re-predicting side-chain conformations. A particular structure may also have atom position clashes, non-ideal bond lengths and angles, and residues with unfavorable energies.

1. Choose Applications > Prime > Refinement from the main window.

   The Refinement panel opens.

There are four refinement tasks available: Refine loops, Predict side chains, Minimize, and Energy Analysis. Refine loops is the default task.

2. Click Load from Workspace.

   The Loops table is populated.

3. In the table of loops, click on the word `loop4`.

   Loop 4, which includes residues 47 through 56, is selected. Markers appear in the Workspace to indicate the location of this loop in the structure.

   Refinement of loops of six or more residues should be performed using extended, not default, sampling. You can change the sampling method in the Structure Refinement Options panel.

   In this exercise, the length of the loop will be edited so that the faster default sampling can be used.

4. Change the beginning residue (Res1) to 53 for `loop4`.

You can edit the table by clicking in a cell and entering a new value.

5. Click the check box for `loop4` in the Run column.
6. Click Start.

   The Refinement - Start dialog box opens.
7. Choose Append new entries as a new group from the Incorporate option menu.
8. Enter `LoopRefinement` in the Name text box.
9. Click Start to launch the job.

   The refinement calculation is started. This job may take 30 minutes. The Monitor panel is displayed and lists the log file.

   When the job finishes, the predicted structure is incorporated into the Project Table and is displayed in the Workspace.

While we have been referring to the calculation that was just performed as a *refinement*, it is more accurately described as a *prediction*. The so-called refinement of loop 53-56 was in fact an ab initio loop prediction, in that the program initially deleted the loop, reconstructed it in a particular way, and then exhaustively sampled it to identify the lowest energy conformation.

Refinement of loops that are less than 9 residues long yield excellent results in a large majority of cases. Loops 10 to 12 residues long yield very good results in a majority of cases. Loops 13 to 15 residues long produce a low energy conformation most of the time, but probably not the global minimum. Loops 16 to 20 residues long produce a low energy conformation, but refinement of loops this long will take on the order of 1-2 days. Loops longer than 20 residues long should not be attempted, partly because of the sampling problem, but also because the run times will be unreasonably long.

2.5.2 Minimizing Target Regions

Since only side chains (not the backbone) of residues within 7.5 Å were sampled during the previous loop refinement, it is not unreasonable to minimize the local environment of the loop before considering refinement complete.

1. In the Refinement panel, choose Minimize from the Task menu.

   To open the panel, choose Applications > Prime > Refinement from the main window.
2. Choose Minimize from the Task menu.
3. Click Select.

   The Atom Selection dialog box is displayed.

4. In the Residue Number text box, enter `53-56` and click Add.
5. Click Proximity.

   The Proximity dialog box is displayed.
6. Type `8.5` in the text box, select Residues, and click OK.
7. Click OK in the Atom Selection dialog box.

   Loop 53-56 and all residues within 8.5 Å are now selected.
8. Click Start.

   The Refinement - Start dialog box opens.
9. Choose Append new entries as a new group from the Incorporate option menu.
10. Enter `LoopMinimization` in the Name text box.
11. Click Start to launch the job.

    When the job finishes, the minimized structure is automatically incorporated into the project. It is now possible to use the refined homology model as input to other Schrödinger programs.

Getting Help

Schrödinger software is distributed with documentation in PDF format. If the documentation is not installed in `$SCHRODINGER/docs` on a computer that you have access to, you should install it or ask your system administrator to install it.

For help installing and setting up licenses for Schrödinger software and installing documentation, see the *Installation Guide*. For information on running jobs, see the *Job Control Guide*.

Maestro has automatic, context-sensitive help (Auto-Help and Balloon Help, or tooltips), and an online help system. To get help, follow the steps below.

- Check the Auto-Help text box, which is located at the foot of the main window. If help is available for the task you are performing, it is automatically displayed there. Auto-Help contains a single line of information. For more detailed information, use the online help.
- If you want information about a GUI element, such as a button or option, there may be Balloon Help for the item. Pause the cursor over the element. If the Balloon Help does not appear, check that Show Balloon Help is selected in the Maestro menu of the main window. If there is Balloon Help for the element, it appears within a few seconds.
- For information about a panel or the tab that is displayed in a panel, click the Help button in the panel, or press F1. The help topic is displayed in your browser.
- For other information in the online help, open the default help topic by choosing Online Help from the Help menu on the main menu bar or by pressing CTRL+H. This topic is displayed in your browser. You can navigate to topics in the navigation bar.

The Help menu also provides access to the manuals (including a full text search), the FAQ pages, the New Features pages, and several other topics.

If you do not find the information you need in the Maestro help system, check the following:

- *Maestro User Manual*, for detailed information on using Maestro
- *Maestro Command Reference Manual*, for information on Maestro commands
- *Maestro Overview*, for an overview of the main features of Maestro
- *Maestro Tutorial*, for a tutorial introduction to basic Maestro features
- *Prime User Manual*, for detailed information on using Prime
- Prime Frequently Asked Questions pages, at https://www.schrodinger.com/Prime_FAQ.html
- Known Issues pages, available on the Support Center.

The manuals are also available in PDF format from the Schrödinger Support Center. Local copies of the FAQs and Known Issues pages can be viewed by opening the file `Suite_2009_Index.html`, which is in the `docs` directory of the software installation, and following the links to the relevant index pages.

Information on available scripts can be found on the Script Center. Information on available software updates can be obtained by choosing Check for Updates from the Maestro menu.

If you have questions that are not answered from any of the above sources, contact Schrödinger using the information below.

E-mail:	help@schrodinger.com
USPS:	Schrödinger, 101 SW Main Street, Suite 1300, Portland, OR 97204
Phone:	(503) 299-1150
Fax:	(503) 299-4532
WWW:	http://www.schrodinger.com
FTP:	ftp://ftp.schrodinger.com

Generally, e-mail correspondence is best because you can send machine output, if necessary. When sending e-mail messages, please include the following information:

- All relevant user input and machine output
- Prime purchaser (company, research institution, or individual)
- Primary Prime user
- Computer platform type
- Operating system with version number
- Prime version number
- mmshare version number

On UNIX you can obtain the machine and system information listed above by entering the following command at a shell prompt:

```
$SCHRODINGER/utilities/postmortem
```

This command generates a file named *username*-*host*-`schrodinger.tar.gz`, which you should send to help@schrodinger.com. If you have a job that failed, enter the following command:

```
$SCHRODINGER/utilities/postmortem jobid
```

where *jobid* is the job ID of the failed job, which you can find in the Monitor panel. This command archives job information as well as the machine and system information, and includes input and output files (but not structure files). If you have sensitive data in the job launch directory, you should move those files to another location first. The archive is named *jobid*-`archive.tar.gz`, and should be sent to help@schrodinger.com instead.

If Maestro fails, an error report that contains the relevant information is written to the current working directory. The report is named `maestro_error.txt`, and should be sent to help@schrodinger.com. A message giving the location of this file is written to the terminal window.

More information on the `postmortem` command can be found in Appendix A of the *Job Control Guide*.

On Windows, machine and system information is stored on your desktop in the file `schrodinger_machid.txt`. If you have installed software versions for more than one release, there will be multiple copies of this file, named `schrodinger_machid-`*N*`.txt`, where *N* is a number. In this case you should check that you send the correct version of the file (which will usually be the latest version).

If Maestro fails to start, send email to help@schrodinger.com describing the circumstances, and attach the file `maestro_error.txt`. If Maestro fails after startup, attach this file and the file `maestro.EXE.dmp`. These files can be found in the following directory:

```
%USERPROFILE%\Local Settings\Application Data\Schrodinger\appcrash
```

Glossary

alignment—The optimal matching of residue positions between sequences, typically a query sequence and one or more template sequences.

anchor—A constraint on alignment set at a given residue position. Alignment changes must preserve the query-template pairing at that residue until the anchor is removed.

ASD—Atom Selection dialog box.

ASL—Atom Specification Language.

button menu—The menu available from a toolbar menu button, which you open by holding down the left mouse button.

Comparative Modeling—Protein structure modeling based on a query-template match with a substantial percentage of identical residues (usually 50% or greater sequence identity).

composite template—A type of template used in the Threading Path, produced from the core (invariable) and variable regions of a family of structurally similar proteins.

constraints—Tools to keep regions of a sequence (alignment constraints) or structure (during minimization) in a particular configuration.

deletions—The residues missing from a query sequence that are present in a template sequence.

entry—A structure or set of structures and associated properties. Entries are represented as a row in the project table, and can be used as input for jobs.

Fold Recognition—The use of secondary structure matching and profiles generated from multiple sequence/structure alignments to find templates when sequence methods are unsuccessful.

gaps—The spaces in an alignment resulting from insertions and deletions.

HETATMs—The atoms of residues, including amino acids, that are not one of the standard 20 amino acids. In PDB files, HETATM.

homolog—A sequence/structure related to the query sequence; i.e., a sequence with many of the same residues in the same patterns as the query sequence. Usually these sequences are derived from the same family and may have similar function.

insertions—The extra residues found in a query sequence that are not found in a template sequence.

loop—A region of undefined secondary structure.

Maestro toolbar—The array of icon buttons which provides tools for common Maestro tasks, located by default along the left side of the main window. There are buttons for operations such as moving structures in the Workspace, changing what is displayed, opening a project, or undoing the most recent Maestro operation.

Main menu bar—The menu bar at the top of the main Maestro window below the Auto-Help window. The main menu bar contains menu titles (Maestro, Project, Edit, etc.) that, when clicked, display menus from which selections can be made.

menu button—A toolbar button that has a menu, which you open by holding down the left mouse button. The button has a black triangle in the lower right corner.

Prime toolbar—The row of icon buttons which provides tools for common Prime tasks, located near the top of the Prime-SP panel.

project—A collection of related data, such as structures with their associated properties. In Prime a project comprises one or more *runs* (executions of the Prime workflow). The project may include data that does not appear in the *project table*.

project table—The Maestro panel associated with a project, featuring a table with rows of entries and columns of properties.

query sequence—A sequence of unknown structure or fold.

Ranking Score—The score used to rank composite templates derived from different seed templates. Generated by the Global Scoring Function in the Threading Path.

refinement—An improvement of a model structure through energy-based optimization of selected regions.

run—A single execution of the Prime workflow using a particular set of choices (of templates, of Paths, and of settings). Each run belongs to a *project*. Runs cannot be saved without saving the project to which they belong.

SSA—Secondary structure assignment.

SSP—Secondary structure prediction.

sequence viewer—An area in which protein sequences are displayed. Right-clicking a sequence opens an *option menu*.There are sequence viewers in the Prime–SP panel and in the Maestro main window. The Prime sequence viewer displays query and template sequences,

including family and conservation data in sequence format, *SSA*s, and *SSP*s. The Workspace sequence viewer displays the sequence and (by default) the SSA for the structures included in the Workspace, provided that they are entries in a named Maestro project.

template sequence—A sequence of known structure and fold used as a basis for building a model of the query.

Threading—A structure prediction process in which *Fold Recognition* is used to define templates, then backbone models are built via alignment to composite templates and refined. May be used when query-template sequence identity is low.

Workspace—The open area in the center of the Maestro main window in which structures are displayed.

Z-Score—Measures the compatibility of the query sequence with the model structure, relative to the compatibility of randomly shuffled sequences of the same composition.

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